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# Collaboration Is Key for Successful Treatment of Youth-Onset Type 2 Diabetes

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## Abstract

Type 2 diabetes (T2D) is increasing in U.S. adolescents, particularly those of ethnic and racial minority groups. Risk factors for youth-onset T2D include obesity, family history of T2D, poor diet, lack of exercise, and poverty. The onset of diabetes-related complications is accelerated in adolescents with T2D compared to adults, and knowledge regarding the optimal way to prevent and slow complications is lacking. Existing treatment options are limited, and research into novel pharmacologic treatments is hindered by lack of sufficient patient population for clinical trials. Health care providers and investigators should collaborate both with each other, and with patients and their communities to build networks that will allow comprehensive evaluation of this disease in order to offer optimal, comprehensive care for these adolescents.

### Keywords

Type 2 diabetes; Adolescents; Complications; Collaboration

Growing up is hard. Growing up with type 2 diabetes (T2D) without suffering long-term physical and psychosocial consequences is close to impossible. A joint consensus conference of the American Diabetes Association, American Academy of Pediatrics, International Society for Pediatric and Adolescent Diabetes, and the Pediatric Endocrine Society was held in 2016 to discuss this concern. The resulting consensus statement, “Youth-Onset Type 2 Diabetes Consensus Report: Current Status, Challenges, and Priorities,” was created with the goal to define the issues that make T2D in youth so challenging and develop solutions to this critical and timely problem [1].

The incidence of youth-onset T2D in the U.S. is increasing at an alarming rate with approximately 5,000 new cases diagnosed per year [2]. The prevalence of T2D in

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adolescents has increased by nearly 31% in the past 15 years, with significantly higher rates among minority groups and females [2,3]. Risk factors for the development of T2D in youth include the physiologic insulin resistance that accompanies the onset of puberty and genetic predisposition, as well as obesity, poor diet, limited physical exercise, and irregular sleep schedules. Although some of these are potentially modifiable risk factors, they are commonplace in adolescents in the U.S. One additional risk factor that is not easily modifiable is the fact that adolescents with T2D have increased rates of poverty and socioeconomic disadvantage. It has been shown that North Americans living in poor areas are 34% more likely to develop obesity and 60% more likely to develop T2D than those living in high-income areas [4]. This increase in youth-onset T2D is concerning, both because adolescents with T2D appear to have more rapid and complete onset of β-cell failure than do adults and because treatment options are severely limited in this patient population [5].

In adults with T2D, microvascular complications such as nephropathy, neuropathy, and retinopathy are associated with duration of diabetes and level of glycemic control. Worrisomely, many adolescents with newly diagnosed T2D have already been found to have evidence of microvascular complications at the time of diagnosis. The TODAY study found that 13% of youth with newly diagnosed T2D already had microalbuminuria [6]. Many also have risk factors for macrovascular complications, including elevated blood pressure in 14% and dyslipidemia in 80%, suggesting differences in the pathophysiology of β-cell dysfunction and insulin resistance in these patients [6].

Not only do youth with T2D appear to develop complications sooner than adults with this disease, the complications evolve more rapidly. One study of First Nations adolescents with T2D found that microvascular complications began to manifest within 5 years after diagnosis and progressed to blindness, end-stage renal disease, and the need for amputation within 10 years [7]. Another concern in youth with T2D is the potential for the disease to affect future generations. Adolescents with diabetes have been found to have higher rates of teen pregnancy—10% compared to the national average of 2.4% [8,9], and babies born to mothers with T2D are more likely to develop metabolic complications and T2D at an earlier age [10].

Undoubtedly, the rising incidence of T2D in adolescents is a serious problem and is complicated by the limited choices of effective treatment options currently available. In adults with T2D, the first-line treatment is lifestyle intervention such as improved nutrition and increased activity. These same interventions have not been well studied in youth with T2D, and the existing data do not show improvement in glycemic control when lifestyle interventions were added to metformin monotherapy [5]. An additional complicating factor for implementing effective lifestyle interventions in youth is that adolescents are part of a family, rather than independent units. They may not have much say in decisions that can affect their health, including type or quality of food purchased, location of meal preparation and consumption, and even the location of their home in regard to safe places to exercise. In order to be successful, lifestyle changes must involve the entire family, and this is often quite difficult to achieve in real-world situations.

Currently, the only pharmacologic treatments approved for children with T2D are metformin and insulin. Although the U.S. Food and Drug Administration has approved over 10 oral and subcutaneous medications for the treatment of T2D in adults, none of these agents have been approved for use in children. One reason for this discrepancy may be related to the Food and Drug Administration requirement that new drugs have safety and efficacy assessments in pediatric populations [11]. Although studies are currently enrolling, there are significant obstacles that limit youth with T2D from enrolling in clinical trials. Reasons for this include socioeconomic causes such as lack of transportation, as well as restrictive eligibility criteria and patient or guardian reluctance to participate [12,13]. Another phenomenon frequently seen in families of adolescents with T2D is the fatalistic view that diabetes is inevitable, and nothing can be done to either reverse or alter its course. These families often decline to participate in research studies because they doubt that any treatment will be effective. Yet another reason for limited participation in ongoing research is that although the incidence of T2D in youth is increasing, there still are not enough patients in the U.S. to fill the large number of clinical trials currently enrolling.

How then, with so many barriers can providers optimize treatment for these patients? The consensus statement offers several solutions [1]. First, investigators should ensure research goals tackle the current knowledge gaps regarding the differences in pathophysiology between children and adults with T2D. There is also a need to better understand the interplay between glycemic control and socioeconomic status in these adolescents. As recruitment is challenging, one solution is to develop multicenter networks to encourage collaboration between investigators and clinicians who have expertise working with pediatric patients with T2D. The Pediatric Diabetes Consortium T2D Registry is one such network that was established in 2012, with initial participation by eight academic pediatric diabetes centers and has now grown to more than 20 sites across the U.S. The goal of this registry is for health care providers to collaborate to improve the care of youth with T2D by developing and sharing best practices and collecting outcome data, as well as advocating for evidence-based improvements in care [14].

There is also a need to develop partnerships between first-line providers who care for high-risk adolescents and those with expertise in caring for youth with T2D. Screening for T2D is important, critically so in high-risk adolescents, and screening rates among primary care providers are currently very low. As poverty and lower socioeconomic status are both risk factors for T2D in youth, community health care providers and free or reduced-cost community clinics are vitally important for screening and diagnosing T2D in these patients. In order to successfully care for these patients, all health care providers must be cognizant of the risk factors for T2D so that adolescents can be diagnosed and referred expeditiously for specialty care.

Youth-onset T2D is a challenging disease not only because of the differences in pathophysiology, but perhaps even more importantly due to the unique challenges that arise in regard to lack of treatment options and difficulty with research study enrollment. As the incidence of T2D in adolescents continues to increase, there is a pressing need to develop new and effective treatments, presented in a way that is attractive and achievable for patients and their families. Growing up with T2D is hard, but if providers and researchers collaborate

to develop novel and effective ways to optimize treatments, it will be much closer to possible.

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